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(12) # EUROPEAN PATENT APPLICATION

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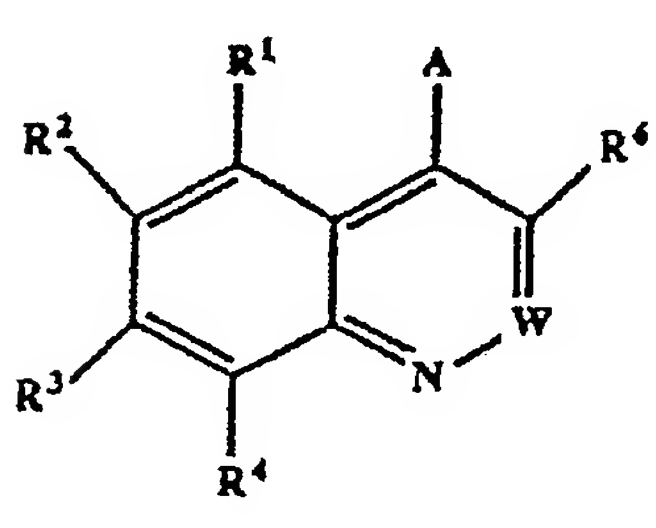
Claims for the following Contracting State: ES.

(54) **Substituted quinolines and cinnolines.**

(57) Compounds of the formula (1):



(1)

wherein:
R^1 to R^4 are independently H, halo, $(C_1\text{-}C_4)$ alkyl, branched $(C_3\text{-}C_4)$ alkyl, halo $(C_1\text{-}C_4)$ alkyl, $(C_1\text{-}C_4)$ alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H, or one of R^2 to R^4 is $-NR^7$-Y-Ar or O-Y-Ar and the rest of R^1 to R^4 are H;
W is N, or CR^5;
R^5 is H, CH_3, Cl, O-Y-Ar, or $-NR^7$-Y-Ar;
R^6 is H, CH_3, Cl or Br;
A is -O-Alk or -X-Y-Ar;
Alk is a $C_2\text{-}C_{18}$ saturated or unsaturated hydrocarbon chain, straight chain or branched, optionally substituted with halo, halo $(C_1\text{-}C_4)$ alkoxy, $(C_3\text{-}C_8)$ cycloalkyl, hydroxy, or acetyl;
X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or O-Y-Ar, then X-Y-Ar is an identical group;
R^7 is H, $(C_1\text{-}C_4)$ alkyl, or acetyl;
R^8 and R^9 are independently H, $(C_1\text{-}C_4)$ alkyl, $(C_1\text{-}C_4)$ acyl, halo, or OH, or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;
Y is an alkylene chain 2 to 8 carbon atoms long, optionally including an O, S, SO, SO_2, or NR^7 group or a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with $(C_1\text{-}C_3)$ alkyl, $(C_2\text{-}C_4)$ alkenyl, phenyl, $(C_3\text{-}C_8)$ cycloalkyl, hydroxy, halo, or $(C_1\text{-}C_4)$ acyl; and
Ar is
1,3-benzodioxolyl
fluorenyl,
pyridyl,
imidazolyl,
indolyl,

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Description

Substituted Quinolines and Cinnolines

Background of the Invention

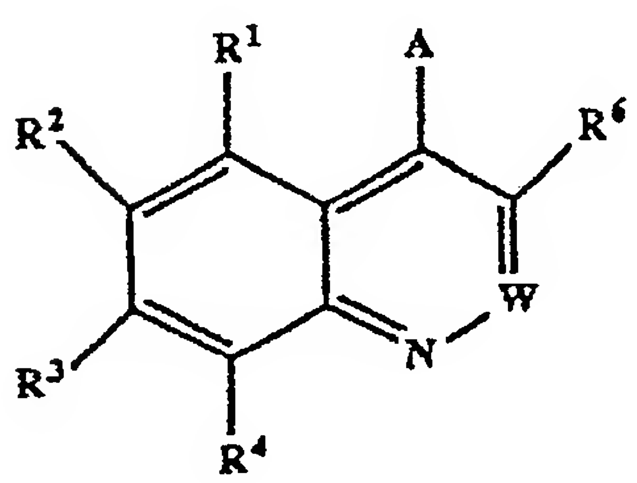
Field of the Invention

This invention provides new compounds that have excellent plant fungicide activity. Some of the compounds have also demonstrated insecticidal and miticidal activity. The invention also provides compositions and combination products that contain a compound of the invention as active ingredient. The invention also provides fungicidal, miticidal, and insecticidal methods.

There is an acute need for new fungicides, insecticides, and miticides, because target pathogens are rapidly developing resistance to currently used pesticides. Widespread failure of N-substituted azole fungicides to control barley mildew was observed in 1983, and has been attributed to the development of resistance. At least 50 species of fungi have developed resistance to the benzimidazole fungicides. The field performance of DMI (demethylation inhibitor) fungicides, which are now widely relied on to protect cereal crops from powdery mildew, has declined since they were introduced in the 1970's. Even recent fungicides, like the acylalanines, which initially exhibited excellent control of potato late blight and grape downy mildew in the field, have become less effective because of widespread resistance. Similarly, mites and insects are developing resistance to the miticides and insecticides in current use. Resistance to insecticides in arthropods is widespread, with at least 400 species resistant to one or more insecticides. The development of resistance to some of the older insecticides, such as DDT, the carbamates, and the organophosphates, is well known. But resistance has even developed to some of the newer pyrethroid insecticides and miticides. Therefore a need exists for new fungicides, insecticides, and miticides.

Summary of the Invention

This invention provides compounds of the formula (1):



(1)

wherein:

R^1 to R^4 are independently

H, halo, $(C_1\text{-}C_4)$ alkyl, branched $(C_3\text{-}C_4)$ alkyl, halo $(C_1\text{-}C_4)$ alkyl, $(C_1\text{-}C_4)$ alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H,

or one of R^2 to R^4 is $-NR^7$-Y-Ar or O-Y-Ar and the rest of R^1 to R^4 are H;

W is N, or CR^5;

R^5 is H, CH_3, Cl, O-Y-Ar, or $-NR^7$-Y-Ar;

R^6 is H, CH_3, Cl or Br;

A is -O-Alk or -X-Y-Ar;

Alk is a $C_2\text{-}C_{18}$ saturated or unsaturated hydrocarbon chain, straight chain or branched, optionally substituted with halo, halo $(C_1\text{-}C_4)$ alkoxy, $(C_3\text{-}C_8)$ cycloalkyl, hydroxy, or acetyl;

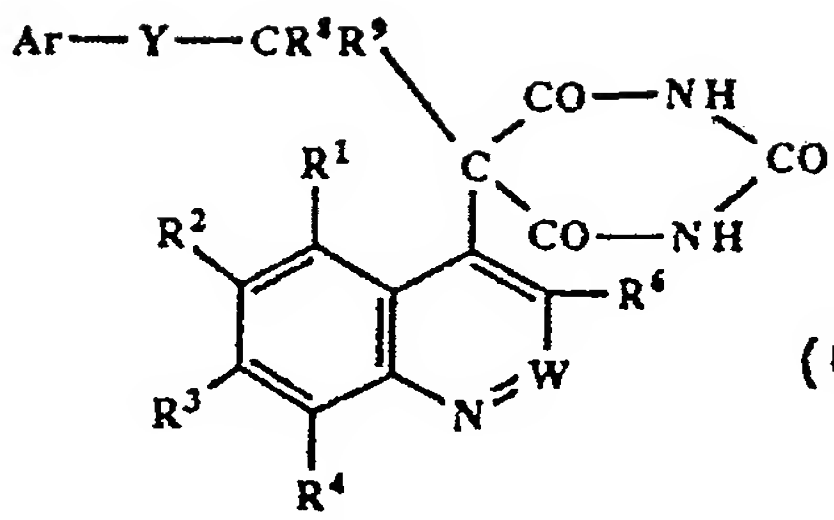
X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or O-Y-Ar, then X-Y-Ar is an identical group;

R^7 is H, $(C_1\text{-}C_4)$ alkyl, or acetyl;

R^8 and R^9 are independently H, $(C_1\text{-}C_4)$ alkyl, $(C_1\text{-}C_4)$ acyl, halo, or OH, or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;

Y is an alkylene chain 2 to 8 carbon atoms long, optionally including an O, S, SO, SO_2, or NR^7 group or a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with $(C_1\text{-}C_3)$ alkyl, $(C_2\text{-}C_4)$ alkenyl, phenyl, $(C_3\text{-}C_8)$ cycloalkyl, hydroxy, halo, or $(C_1\text{-}C_4)$ acyl; and

Ar is



(6)

to provide a compound of formula (1) wherein A is -CR^8R^9Y-Ar; or

(e) halogenating a compound of formula (1) wherein R^6 is H with $POCl_3/PCl_5$ to provide a compound of formula (1) wherein R^6 is Cl; or

(f) reacting a compound of formula (1) wherein R^6 is H with Br_2 in acetic acid to provide a compound of formula (1) wherein R^6 is Br; or

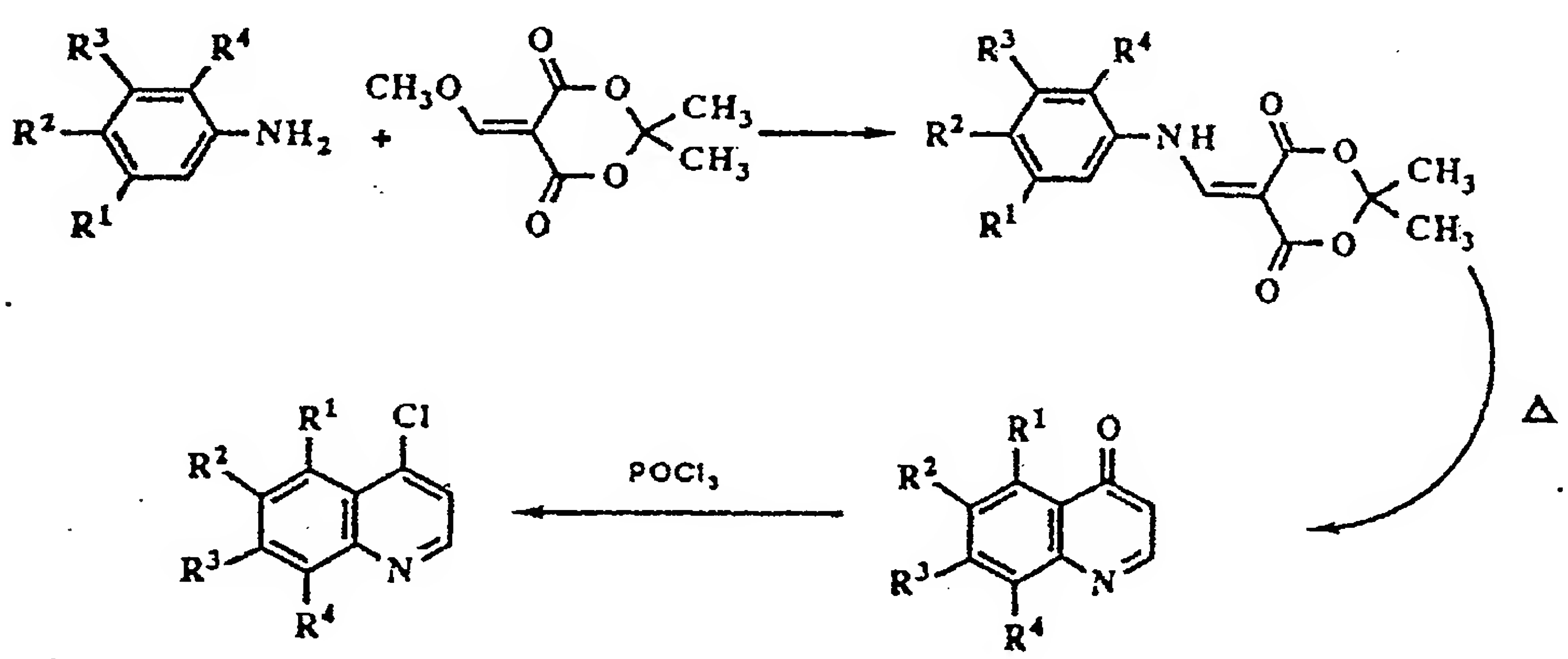
(g) oxidizing a compound of formula (1) wherein W is CR^5 to provide the corresponding N-oxide.

Preparation of Quinoline Starting Materials

Quinoline starting materials can be synthesized using a variety of known procedures.

Organic Syntheses, collective volume 3, 1955, pp. 272-75, gives a procedure for preparing 4,7-dichloroquinoline, and other polysubstituted quinolines. Another general procedure is described in Tetrahedron, vol. 41, pp. 3033-36 (1985).

Many of the quinoline starting materials used in the following examples were prepared by the protocol shown in the following reaction scheme



In cases where mixtures of isomeric products were obtained, the mixture of substituted 4-quinolones was chlorinated under standard conditions, and the 4-chloroquinolines were separated by liquid chromatography.

Preparation of Cinnoline Starting Materials

Cinnoline analogs are prepared via published methods. (C. M. Atkinson and J. C. Simpson - J. Chem. Soc. London, 1947, 232). The substituted 2-amino-acetophenone is diazotized at 0-5°C in water using sodium nitrite and mineral acid, and the intermediate diazonium salt is trapped by the enolic component of the ketone to provide the requisite 4-hydroxycinnoline. Routine chlorination provides the desired intermediates.

EXAMPLES 1 TO 295

Tables 1-12 identify compounds actually prepared by the above described general procedures, and give each compound's melting point. Specific illustrative preparations of the compounds of Examples 4, 10, 25, 69, 97, 154, 159, 173, 181, 186, 209, 212, 221, 238, 251, and 261 follow the table.

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
97	8-fluoro-N-[2-[2-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine	157-158°C
98	2-chloro-N-[2-(2,4-dichlorophenyl)ethyl]-8-fluoro-4-quinolinamine	199-200°C
99	N-(2-phenylethyl)-8-(trifluoromethyl)-4-quinolinamine	151-152°C
100	7-chloro-N-[2-(2-methoxyphenyl)ethyl]-4-quinolinamine	140-142°
101	7-chloro-N-[2-(3,4-dichlorophenyl)ethyl]-4-quinolinamine	128-130°C
102	N-[2-(4-chlorophenyl)ethyl]-2-methyl-4-quinolinamine	176-178°C
103	N-[2-(2-chloro-6-fluorophenyl)ethyl]-8-fluoro-4-quinolinamine	198-201°C
104	N-[2-(2,4-dichlorophenyl)ethyl]-7-(trifluoromethyl)-4-quinolinamine	175-177°C
105	N-[2-(4-chlorophenyl)ethyl]-N-ethyl-8-fluoro-4-quinolinamine	oil
106	7-chloro-N-(4-fluorophenyl)-N-methyl-4-quinolinamine	83-85°C
107	7-chloro-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine	184-186°C